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(54) Title: FOLDABLE OPHTHALMIC AND OTORHINOLARYNGOLOGICAL DEVICE MATERIALS

(57) Abstract: Disclosed are soft, high refractive index, acrylic materials having an elongation of at least 150 %. These materials, especially useful as intraocular lens materials, contain an aryl acrylic hydrophobic monomer as the single principal device-forming monomer. In addition to their use as intraocular lens materials, the present materials are also suitable for use in other ophthalmic or otorhinolaryngological devices, such as contact lenses, keratoprostheses, corneal inlays or rings; otological ventilation tubes and nasal implants.

FOLDABLE OPHTHALMIC AND OTORHINOLARYNGOLOGICAL DEVICE MATERIALS

5 Field of the Invention

This invention is directed to acrylic device materials. In particular, this invention relates to soft, high refractive index acrylic device materials particularly suited for use as intraocular lens ("IOL") materials.

10

Background of the Invention

With the recent advances in small-incision cataract surgery, increased emphasis has been placed on developing soft, foldable materials suitable for use in artificial lenses. In general, these materials fall into one of three categories: hydrogels, silicones, and acrylics.

In general, hydrogel materials have a relatively low refractive index, making them less desirable than other materials because of the thicker lens optic necessary to achieve a given refractive power. Silicone materials generally have a higher refractive index than hydrogels, but tend to unfold explosively after being placed in the eye in a folded position. Explosive unfolding can potentially damage the corneal endothelium and/or rupture the natural lens capsule. Acrylic materials are desirable because they typically have a high refractive index and unfold more slowly or controllably than silicone materials.

U.S. Patent No. 5,290,892 discloses high refractive index, acrylic materials suitable for use as an IOL material. These acrylic materials contain, as principal components, two aryl acrylic monomers. They also contain a cross-linking component. The IOLs made of these acrylic materials can be rolled or folded for insertion through small incisions.

U.S. Patent No. 5,331,073 also discloses soft acrylic IOL materials. These materials contain as principal components, two acrylic monomers

which are defined by the properties of their respective homopolymers. The first monomer is defined as one in which its homopolymer has a refractive index of at least about 1.50. The second monomer is defined as one in which its homopolymer has a glass transition temperature less than about 22 °C.

5 These IOL materials also contain a cross-linking component. Additionally, these materials may optionally contain a fourth constituent, different from the first three constituents, which is derived from a hydrophilic monomer. These materials preferably have a total of less than about 15% by weight of a hydrophilic component.

10

U.S. Patent No. 5,693,095 discloses foldable ophthalmic lens materials comprising a total of at least 90% by weight of only two principal lens-forming monomers. One lens-forming monomer is an aryl acrylic hydrophobic monomer. The other lens-forming monomer is a hydrophilic monomer. The lens materials also comprise a cross-linking monomer and optionally
15 comprise a UV absorber, polymerization initiators, reactive UV absorbers and reactive blue-light absorbers.

Summary of the Invention

20

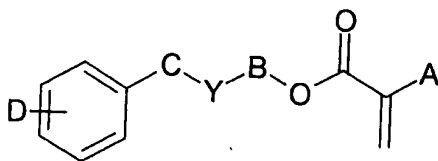
Improved soft, foldable acrylic materials which are particularly suited for use as IOLs, but which are also useful as other ophthalmic or otorhinolaryngological devices, such as contact lenses, keratoprotheses, corneal rings or inlays, otological ventilation tubes and nasal implants have
25 now been discovered. These materials contain only one principal lens-forming component: an aryl acrylic hydrophobic monomer. The materials of the present invention comprise at least about 80% by weight of the principal monomeric component. The remainder of the material comprises a cross-linking monomer and optionally one or more additional components selected
30 from the group consisting of UV-light absorbing compounds and blue-light absorbing compounds.

Among other factors, the present invention is based on the finding that acrylic copolymers suitable for use as foldable IOL materials can be synthesized using only one principal aryl acrylic hydrophobic monomer, reducing or eliminating difficulties, such as physico/chemical heterogeneity, associated with curing copolymers that contain two or more principal device-forming monomers.

Detailed Description of the Invention

The ophthalmic or otorhinolaryngological device materials of the present invention comprise only one principal device-forming monomer. For convenience, the device-forming monomer may be referred to as a lens-forming monomer, particularly with reference to an IOL. The materials of the present invention, however, are also suitable for use as other ophthalmic or otorhinolaryngological devices such as contact lenses, keratoprotheses, corneal inlays or rings, otological ventilation tubes and nasal implants.

The aryl acrylic hydrophobic monomers suitable for use as the sole lens-forming monomer in the materials of the present invention have the formula



(I)

wherein: A is H, CH₃, CH₂CH₃, or CH₂OH;

B is (CH₂)_m or [O(CH₂)₂]_n;

C is (CH₂)_w;

m is 2 – 6;

n is 1 – 10;

Y is nothing, O, S, or NR, provided that if Y is O, S, or NR, then B is (CH₂)_m;

R is H, CH₃, C_nH_{2n+1} (n=1-10), iso-OC₃H₇, C₆H₅, or
CH₂C₆H₅;

w is 0 – 6, provided that m + w ≤ 8; and

D is H, C₁ – C₄ alkyl, C₁ – C₄ alkoxy, C₆H₅, CH₂C₆H₅ or halogen.

5 Preferred aryl acrylic hydrophobic monomers for use in the materials of the present invention are those wherein A is CH₃, B is (CH₂)_m, m is 2 - 5, Y is nothing or O, w is 0 – 1, and D is H. Most preferred are 4-phenylbutyl methacrylate, 5-phenylpentyl methacrylate, 2-benzyloxyethyl methacrylate,
10 and 3-benzyloxypropyl methacrylate.

Monomers of structure I can be made by known methods. For example, the conjugate alcohol of the desired monomer can be combined in a reaction vessel with methyl methacrylate, tetrabutyl titanate (catalyst), and a
15 polymerization inhibitor such as 4-benzyloxy phenol. The vessel can then be heated to facilitate the reaction and distill off the reaction by-products to drive the reaction to completion. Alternative synthesis schemes involve adding methacrylic acid to the conjugate alcohol and catalyzing with a carbodiimide or mixing the conjugate alcohol with methacryloyl chloride and a base such as
20 pyridine or triethylamine.

The materials of the present invention comprise a total of at least about 80%, preferably at least about 85%, by weight or more of the principal lens-forming monomer.

25 The copolymer materials of the present invention are cross-linked. The copolymerizable cross-linking agent used in the copolymers of this invention may be any terminally ethylenically unsaturated compound having more than one unsaturated group. Suitable cross-linking agents include, for example:
30 ethylene glycol dimethacrylate; diethylene glycol dimethacrylate; allyl methacrylate; 1,3-propanediol dimethacrylate; 2,3-propanediol dimethacrylate; 1,6-hexanediol dimethacrylate; 1,4-butanediol dimethacrylate; CH₂=C(CH₃)C(=O)O-(CH₂CH₂O)_n-C(=O)C(CH₃)=CH₂ where n = 1 – 50; and

CH₂=C(CH₃)C(=O)O(CH₂)_tO-C(=O)C(CH₃)=CH₂ where t = 3 - 20; and their corresponding acrylates. The most preferred cross-linking monomer is CH₂=C(CH₃)C(=O)O-(CH₂CH₂O)_n-C(=O)C(CH₃)=CH₂ where n is such that the number-average molecular weight is about 400, about 600, or, most preferably, about 1000.

The chosen cross-linking agent should be soluble in the chosen monomer of structure I to minimize curing problems. When n approaches the upper end of the range of 1 - 50, the CH₂=C(CH₃)C(=O)O-(CH₂CH₂O)_n-C(=O)C(CH₃)=CH₂ cross-linker may not be soluble at desired levels in some monomers of structure I, even with the aid of heat or sonication.

Generally, only one cross-linking monomer will be present in the device materials of the present invention. In some cases, however, combinations of cross-linking monomers may be desirable. If combinations of two or more types of cross-linking agents are used, none of the cross-linking agents may be CH₂=C(CH₃)C(=O)O-(CH₂CH₂O)_n-C(=O)C(CH₃)=CH₂ wherein n = 2-50.

Generally, the total amount of the cross-linking component is at least 0.1% by weight and, depending on the identity and concentration of the remaining components and the desired physical properties, can range to about 20% by weight. The preferred concentration range for the cross-linking component is 0.1 - 15% by weight.

In addition to the aryl acrylic hydrophobic lens-forming monomer and the cross-linking component, the lens material of the present invention may also contain a total of up to about 10% by weight of additional components which serve other purposes, such as reactive UV and/or blue-light absorbers.

A preferred reactive UV absorber is 2-(2'-hydroxy-3'-methallyl-5'-methylphenyl)benzotriazole, commercially available as o-Methallyl Tinuvin P

("oMTP") from Polysciences, Inc., Warrington, Pennsylvania. UV absorbers are typically present in an amount from about 0.1 - 5 % (weight).

Suitable reactive blue-light absorbing compounds are those described in U.S. Patent No. 5,470,932, the entire contents of which are hereby incorporated by reference. Blue-light absorbers are typically present in an amount from about 0.01 - 0.5 % (weight).

Suitable polymerization initiators include thermal initiators and photoinitiators. Preferred thermal initiators include peroxy free-radical initiators, such as t-butyl (peroxy-2-ethyl)hexanoate and di-(tert-butylcyclohexyl) peroxydicarbonate (commercially available as Perkadox[®] 16 from Akzo Chemicals Inc., Chicago, Illinois). Particularly in cases where the lens material does not contain a blue-light absorbing chromophore, preferred photoinitiators include benzoylphosphine oxide photoinitiators, such as the blue-light initiator 2,4,6-trimethyl-benzoyldiphenylphosphine oxide, commercially available as Lucirin[®] TPO from BASF Corporation (Charlotte, North Carolina). Initiators are typically present in an amount of about 5% (weight) or less.

The identity and amount of the principal lens-forming monomer described above and the identity and amount of any additional components are determined by the desired properties of the finished ophthalmic lens. Preferably, the ingredients and their proportion are selected so that the acrylic lens materials of the present invention possess the following properties, which make the materials of the present invention particularly suitable for use in IOLs which are to be inserted through incisions of 5 mm or less.

The lens material preferably has a refractive index in the dry state of at least about 1.50 as measured by an Abbe' refractometer at 589 nm (Na light source). For a given optic diameter, optics made from materials having a refractive index lower than 1.50 are necessarily thicker than optics of the same power which are made from materials having a higher refractive index. As

such, IOL optics made from materials having a refractive index lower than about 1.50 generally require relatively larger incisions for IOL implantation.

5 The glass-transition temperature ("T_g") of the lens material, which affects the material's folding and unfolding characteristics, is preferably below about 25 °C, and more preferably below about 15 °C. T_g is measured by differential scanning calorimetry at 10 °C/min., and is determined at the midpoint of the transition of the heat flux curve.

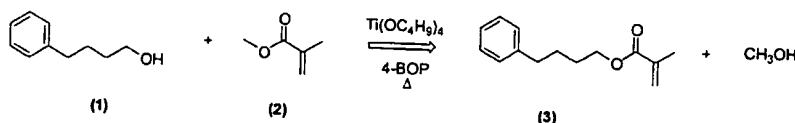
10 The lens material will have an elongation of at least 150%, preferably at least 200%, and most preferably at least 300%. This property indicates that the lens generally will not crack, tear or split when folded. Elongation of polymer samples is determined on dumbbell shaped tension test specimens with a 20 mm total length, length in the grip area of 4.88 mm, overall width of 2.49 mm, 15 0.833 mm width of the narrow section, a fillet radius of 8.83 mm, and a thickness of 0.9 mm. Testing is performed on samples at standard laboratory conditions of 23 ± 2 °C and 50 ± 5 % relative humidity using a tensile tester. The grip distance is set at 14 mm and a crosshead speed is set at 500 mm/minute and the sample is pulled to failure. The elongation (strain) is 20 reported as a fraction of the displacement at failure to the original grip distance. The modulus is calculated as the instantaneous slope of the stress-strain curve at a selected strain. Stress is calculated at the maximum load for the sample, typically the load when the sample breaks, assuming that the initial area remains constant. This stress is recorded as "tensile strength" in 25 the examples below.

IOLs constructed of the materials of the present invention can be of any design capable of being rolled or folded into a small cross section that can fit through a relatively smaller incision. For example, the IOLs can be of what is 30 known as a one piece or multipiece design, and comprise optic and haptic components. The optic is that portion which serves as the lens. The haptics are attached to the optic and hold the optic in its proper place in the eye. The

optic and haptic(s) can be of the same or different material. A multipiece lens is so called because the optic and the haptic(s) are made separately and then the haptics are attached to the optic. In a single piece lens, the optic and the haptics are formed out of one piece of material. Depending on the material, the haptics are then cut, or lathed, out of the material to produce the IOL.

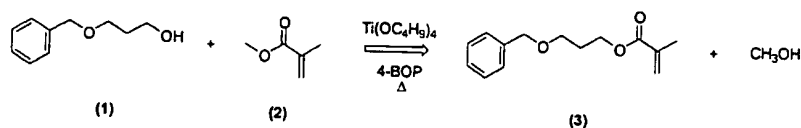
The invention will be further illustrated by the following examples, which are intended to be illustrative, but not limiting.

Example 1: Synthesis of 4-phenylbutyl methacrylate.



A three neck round bottom flask containing a teflon coated magnetic stirring bar was successively charged with 120 mL (1.09 mol) of methyl methacrylate (2), 5.35 g (0.015 mol) of titanium tetrabutoxide ($\text{Ti(OC}_4\text{H}_9)_4$), 60 mL (0.39 mol) of 4-phenyl-1-butanol (1), and 14.6 g (0.073 mol) of 4-benzyloxyphenol (4-BOP). An addition funnel, thermometer, and a short path still head with thermometer and receiver flask were placed in the flask necks. The flask was placed in an oil bath and the temperature was increased until distillation began. Methyl methacrylate (2) was placed in the addition funnel and was added dropwise at the same rate as the distillate. The reaction mixture was heated for 4 hours and then cooled to room temperature. The crude product was vacuum distilled to isolate 62.8 g (0.29 mol, 74%) of 4-phenylbutyl methacrylate (3) as a clear, colorless liquid.

Example 2: Synthesis of 3-benzyloxypropyl methacrylate.



A three neck round bottom flask containing a teflon coated magnetic stirring
 bar was successively charged with 95 mL (0.884 mol) of methyl methacrylate
 (2), 4.22 g (0.012 mol) of titanium tetrabutoxide ($\text{Ti}(\text{OC}_4\text{H}_9)_4$), 50 mL (0.316
 mol) of 3-benzyloxy-1-propanol (1), and 14.6 g (0.073 mol) of 4-
 benzyloxyphenol (4-BOP). An addition funnel, thermometer, and a short path
 still head with thermometer and receiver flask were placed in the flask necks.
 The flask was placed in an oil bath and the temperature was increased until
 distillation began. Methyl methacrylate (2) was placed in the addition funnel
 and was added dropwise at the same rate as the distillate. The reaction
 mixture was heated for 4 hours and then cooled to room temperature. The
 crude product was vacuum distilled to isolate 36.5 g (0.156 mol, 49%) of 3-
 benzyloxypropyl methacrylate (3) as a clear, colorless liquid.

Examples 3 - 29, shown below in Tables 1 - 4, illustrate of the materials of the
 present invention. Each of the formulations of Examples 3 - 29 are prepared
 as follows. After combining the formulation components as listed in Tables 1 -
 4, each formulation is mixed by agitation and then injected into a
 polypropylene 25 x 12 x 1 mm slab mold. To make slabs, the cavity in the
 bottom portion of the slab mold is filled to capacity with the formulation and
 then the top is placed on strictly as a seal. The molds can either be filled
 under an inert nitrogen or standard laboratory atmosphere. To maintain the
 mold geometry during curing, spring clamps are used on the molds. The
 clamped molds are placed in a forced air oven and cured by heating to 70 -
 80 °C, holding at 70 - 80 °C for one hour, then heating to approximately 100 -
 110 °C and holding at approximately 100 - 110 °C for two hours. At the end

of polymerization period, the molds are opened and the cured intraocular lenses or polymer slabs are removed and extracted in acetone to remove any materials not bound to the cross-linked network.

5 Physical property data shown for the cured materials in Tables 1 - 4 were assessed (according to the methods referred to above). Unless indicated otherwise, all ingredient amounts shown below are listed as % by weight. The following abbreviations are used in Tables 1-4:

10 PEMA: 2-phenylethyl methacrylate
 PPrMA: 3-phenylpropylmethacrylate
 PBMA: 4-phenylbutylmethacrylate
 BEEMA: benzyloxyethoxyethyl methacrylate
 BEMA: 2-benzyloxyethyl methacrylate
 15 BPMA: 3-benzyloxypropyl methacrylate
 PPMA: 5-phenylpentyl methacrylate
 BBMA: 4-benzyloxybutyl methacrylate
 PEO 1000: polyethylene glycol 1000 dimethacrylate
 PEO 600: polyethylene glycol 600 dimethacrylate
 20 PEO 400: polyethylene glycol 400 dimethacrylate
 EGDMA: ethylene glycol dimethacrylate
 t-BPO: t-butyl (peroxy-2-ethyl)hexanoate
 BPO: benzoyl peroxide

25

TABLE 1

Example No.	PEMA	PPrMA	PBMA	PEO 1000	EGDMA	t-BPO	%Elongation	Tg (°C)
3	85			15		1	304	—
4		99			1	1	172	15
5		85		15		1	753	-10
6			99		1	1	583	0
7			85	15		1	619	-24

TABLE 2

Component	Examples						
	8	9	10	11	12	13	14
BEMA	-	-	-	-	-	89.9	-
PBMA	-	-	-	-	-	-	90.0
BPMA	94.7	90	-	99.6	-	-	-
PPMA	-	-	89.7	-	-	-	-
BBMA	-	-	-	-	89.9	-	-
PEO 1000	5.3	10	10.3	-	10.1	10.1	10.1
EGDMA	-	-	-	0.4	-	-	-
t-BPO	1.4	1.5	1.4	1.6	1.6	1.3	1.4
Tensile strength (MPa)	3.37	2.83	2.02	3.07	1.11	6.46	4.195
% Strain	900	659	515	974	440	815	696
Young's modulus (MPa)	0.67	0.62	0.76	1.02	0.33	1.89	2.00
100% modulus (MPa)	0.45	0.42	0.51	0.59	0.22	1.07	0.99
RI (dry)	1.539	1.534	1.533	1.543	1.531	1.541	1.535

5

TABLE 3

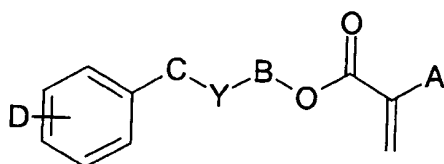
Component	Examples								
	15	16	17	18	19	20	21	22	23
PBMA	89.75	85.02	79.97	94.95	89.82	85.03	94.99	89.89	84.96
PEO 400	10.25	14.98	20.03	---	---	---	---	---	---
PEO 600	---	---	---	5.05	10.18	14.97	---	---	---
PEO 1000	---	---	---	---	---	---	5.01	10.11	15.04
BPO	0.98	0.96	0.95	0.98	0.95	0.96	1.04	0.95	0.97
Tensile Strength (MPa)	8.23	8.6	8.74	6.55	6.33	5.14	6.17	5.62	4.35
% Strain	444	378	325	881	707	562	1051	875	699
Young's modulus (MPa)	6.59	5.78	---	---	---	---	---	---	---
100% modulus (MPa)	3.47	3.34	5.56	3.85	2.82	1.77	4.05	1.92	1.24
Tg (°C)	5	4	3.32	2.28	1.55	1.12	2.06	1.12	0.77
	5	4	-1	-1	-5	---	---	---	---

TABLE 4

Component	Examples (Ingredients shown in % w/w)							
	24	25	26	27	28	29	30	31
BEEMA	---	---	---	---	---	---	---	---
PPrMA	85.03	---	---	85.00	---	---	99.6	90.0
PBMA	---	85.02	---	---	84.94	---	---	---
PPMA	---	---	85.06	---	---	85.00	---	---
PEO 600	14.97	14.98	14.94	---	---	---	---	---
PEO 1000	---	---	---	15.00	15.06	15.00	---	10.0
EGDMA	---	---	---	---	---	---	0.6	---
BPO	1.00	1.01	0.99	1.01	1.01	1.01	---	---
t-BPO	---	---	---	---	---	---	1.1	1.2
Tensile Strength (MPa)	8.34	4.24	2.67	6.15	3.35	2.05	1.56	1.22
% Strain	502	486	390	662	582	402	468	294
Youngs (MPa)	5.48	1.38	0.85	2.41	0.88	0.67	0.32	0.51
100% (MPa)	3.09	0.96	0.57	1.41	0.63	0.48	0.24	0.36
Tg (°C)	---	---	---	---	---	---	-23.2	-26.7

We claim:

1. A polymeric ophthalmic or otorhinolaryngological device material having an elongation of at least 150%, comprising a single device-forming monomer and a cross-linking monomer, wherein the single device-forming monomer is present in an amount of at least about 80% by weight and is an aryl acrylic hydrophobic monomer of the formula



(I)

wherein: A is H, CH₃, CH₂CH₃, or CH₂OH;

B is (CH₂)_m or [O(CH₂)₂]_n;

C is (CH₂)_w;

m is 2 – 6;

n is 1 – 10;

Y is nothing, O, S, or NR, provided that if Y is O, S, or NR, then B is (CH₂)_m;

R is H, CH₃, C_nH_{2n+1} (n=1-10), iso-OC₃H₇, C₆H₅, or CH₂C₆H₅;

w is 0 – 6, provided that m + w ≤ 8; and

D is H, C₁ – C₄ alkyl, C₁ – C₄ alkoxy, C₆H₅, CH₂C₆H₅ or halogen.

2. The polymeric ophthalmic or otorhinolaryngological device material of claim 1 wherein A is CH₃, B is (CH₂)_m, m is 2 - 5, Y is nothing or O, w is 0 – 1, and D is H.

3. The polymeric ophthalmic or otorhinolaryngological device material of Claim 2 wherein the aryl acrylic hydrophobic monomer is selected from the group consisting of 4-phenylbutyl methacrylate; 5-phenylpentyl

methacrylate; 2-benzyloxyethyl methacrylate; and 3-benzyloxypropyl methacrylate.

4. The polymeric ophthalmic or otorhinolaryngological device material of Claim 1 further comprising one or more components selected from the group consisting of reactive UV absorbers and reactive blue-light absorbers.
5. The polymeric ophthalmic or otorhinolaryngological device material of Claim 1 wherein the material is an ophthalmic device material and has a refractive index of at least 1.50.
6. The polymeric ophthalmic or otorhinolaryngological device material of Claim 1 wherein the material has a Tg less than about +25 °C.
7. The polymeric ophthalmic or otorhinolaryngological device material of Claim 6 wherein the material has a Tg less than about +15 °C.
8. The polymeric ophthalmic or otorhinolaryngological device material of Claim 1 wherein the material has an elongation of at least 200%.
9. The polymeric ophthalmic or otorhinolaryngological device material of Claim 8 wherein the copolymer has an elongation of at least 300%.
10. The polymeric ophthalmic or otorhinolaryngological device material of Claim 1 wherein the device is selected from the group consisting of contact lenses; keratoprotheses; corneal inlays or rings; otological ventilation tubes; and nasal implants.
11. The polymeric ophthalmic or otorhinolaryngological device material of Claim 1 wherein the cross-linking component comprises one or more cross-linking agents selected from the group consisting of ethylene

glycol dimethacrylate; diethylene glycol dimethacrylate; allyl methacrylate; 1,3-propanediol dimethacrylate; 2,3-propanediol dimethacrylate; 1,6-hexanediol dimethacrylate; 1,4-butanediol dimethacrylate; $\text{CH}_2=\text{C}(\text{CH}_3)\text{C}(=\text{O})\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{C}(=\text{O})\text{C}(\text{CH}_3)=\text{CH}_2$ where $n = 1 - 50$; $\text{CH}_2=\text{C}(\text{CH}_3)\text{C}(=\text{O})\text{O}(\text{CH}_2)_t\text{OC}(=\text{O})\text{C}(\text{CH}_3)=\text{CH}_2$ where $t = 3 - 20$; and their corresponding acrylates, provided that if the device material comprises two or more cross-linking agents, none of the cross-linking agents is $\text{CH}_2=\text{C}(\text{CH}_3)\text{C}(=\text{O})\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{C}(=\text{O})\text{C}(\text{CH}_3)=\text{CH}_2$ wherein $n = 2-50$.

12. The polymeric ophthalmic or otorhinolaryngological device material of Claim 1 wherein the single device-forming monomer is present in an amount of at least about 85% by weight.
13. The polymeric ophthalmic or otorhinolaryngological device material of Claim 1 wherein the cross-linking monomer is present in an amount of about 0.01 - 15% by weight.
14. The polymeric ophthalmic or otorhinolaryngological device material of Claim 1 wherein the aryl acrylic hydrophobic monomer is selected from the group consisting of 4-phenylbutyl methacrylate; 5-phenylpentyl methacrylate; 2-benzyloxyethyl methacrylate; and 3-benzyloxypropyl methacrylate; and the cross-linking monomer is $\text{CH}_2=\text{C}(\text{CH}_3)\text{C}(=\text{O})\text{O}-(\text{CH}_2\text{CH}_2\text{O})_n-\text{C}(=\text{O})\text{C}(\text{CH}_3)=\text{CH}_2$, where n is such that the number average molecular weight of the cross-linking monomer is about 1000.
15. An intraocular lens optic comprising the polymeric device material of Claim 1.
16. An intraocular lens optic comprising the polymeric device material of Claim 14.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/23283

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C08F220/30 C08F220/18 G02B1/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C08F G02B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 433 746 A (NAMDARAN FARHAD H ET AL) 18 July 1995 (1995-07-18) claims 1,2 ---	1
A	US 5 922 821 A (KARAKELLE MUTLU ET AL) 13 July 1999 (1999-07-13) claims 1-17 ---	1
A	US 5 290 892 A (NAMDARAN FARHAD H ET AL) 1 March 1994 (1994-03-01) cited in the application claims 1-7 column 2, line 16 - line 39 column 7; tables 1,2 --- -/--	1

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

31 October 2000

Date of mailing of the international search report

14/12/2000

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INTERNATIONAL SEARCH REPORT

Interr. nal Application No
PCT/US 00/23283

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	US 5 693 095 A (JINKERSON DAVID L ET AL) 2 December 1997 (1997-12-02) cited in the application claims 1-29 column 1, line 52 -column 2, line 3 column 2, line 32 - line 38 column 2, line 44 -column 3, line 38 -----	1
P,A	WO 99 53347 A (ALCON LAB INC) 21 October 1999 (1999-10-21) claims 1-7 -----	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

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